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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,114	06/22/2001	Seung-Ho Choi	13764-007001	9054

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/888,114	Applicant(s) CHOI ET AL.	
	Examiner Zachariah Lucas	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3 and 5-22* is/are pending in the application.

4a) Of the above claim(s) *6-11 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,12 and 14-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6, 12
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, subgroup B, and the species wherein the biopolymer is carrageenan in Paper No. 10 is acknowledged.

2. Claims 6-11, 13, 15, and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10

Priority

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior non-provisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 2,3,5, 12, and 14-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 8-11, 14-21, 24, 31, and 32-34 of U.S. Patent No. 6,248,360. The rejected claims read on a pharmaceutical composition comprising a biopolymer, a cephalosporin, a metal cation, and an absorption enhancer. Although the conflicting claims are not identical, they are not patentably distinct from each other because the currently claimed compositions represent a subset of the compositions claimed in the patent. As this subset, and several embodiments thereof, is described by the patent claims, the presently claimed material is obvious therefrom.

It is noted that the '360 patent does not specifically claim a pharmaceutical composition that comprises an adsorption enhancer. However, several of the examples of the claimed subject matter in the patent disclose compositions comprising capmul. See e.g. Example 7, column 8; Examples 8 and 9, column 9; Examples 10 and 11, column 10; and Example 12, column 11. Capmul is identified by the patent as an adsorption enhancer. Col. 8, lines 61-64. Because the

specification of the prior patent discloses embodiments comprising the enhancer, this constitutes an obvious variation of the claimed composition.

It is also noted that the patent does not disclose the subject matter of claim 21. This is not deemed important as the selection of a particular biopolymer would have been obvious as the selection of the optimal calcium content of the biopolymer. Also, in the specification of the present application, the carrageenan disclosed as meeting the claimed limitation is a known and commercially available carrageenan. Page 24, lines 19-20. It would have been obvious to one of ordinary skill in the art to use a commercially available carrageenan in the composition claimed by the patent.

6. The above rejection is, in part, based on the specification of a previously issued patent, rather than the claims. In support of the use of this material, the examiner notes the following excerpt from MPEP section 804:

> When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. This does not mean that one is precluded from all use of the patent disclosure.
>
> The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

Thus, the courts have held that it is permissible to use the specification in determining what is included in, and obvious from, the invention defined by the claim on which the rejection is based. This is true even where elements are drawn from the specification describing the claimed invention which are not elements in the claim itself.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 2, 3, 5, 12, 14-16, 19, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Choi et al., U.S. Patent No. 6,248,360. The claims of the patent claim similar and overlapping subject matter with the present application. Further, examples 7 and 8 of the patent teach embodiments of the rejected claims.

The applied reference has a common inventor and a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 2, 3, 5, 12, and 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choi et al., U.S. Patent No. 6,248,360 for substantially the same reasons as indicated in the double patenting rejection, and the anticipation rejection, of the present claims over this reference as described above.

11. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choi et al., U.S. Patent No. 6,248,360, in view of Watts et al., U.S. Patent 6,465,626. Claim 22 describes a pharmaceutical composition. The rejected claim reads on a pharmaceutical composition comprising a biopolymer, a cephalosporin, a metal cation, and an absorption enhancer, wherein the enhancer is a non-ionic surfactant. Choi has been described above. This reference does not teach the claimed invention wherein the enhancer is a non-ionic surfactant.

Watts teaches that the inclusion of an absorption enhancer is effective in increasing the adsorption of polar molecules across mucosal membranes. Col. 1, lines 10-28. The reference further teaches that among the enhancers known in the art are non-ionic surfactants. Id. It would

therefore have been obvious to one of ordinary skill in the art to substitute the enhancers taught in Watts for the enhancer disclosed in Choi.

12. Claims 2, 3, 5, 12, 14-19, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scott et al., U.S. Patent 6,458,287, in view of Watts. Claim 2 describes a pharmaceutical composition comprising a biopolymer, a cephalosporin, a metal cation, and an absorption enhancer. The remaining claims further define the four components, or the interactions among them.

Scott teaches microspheres for the delivery of therapeutics into a person. See e.g., column 10, lines 5-17. Among the methods of administration by which the described microspheres deposit the therapeutics is through oral and mucosal routes. Id. These microspheres comprise a macromolecule, a water-soluble polymer, first and second complexing agents, and an active agent. See e.g., col. 19, lines 19-29. Exemplary water-soluble polymers are disclosed in columns 17 and 18 of the specification. These include polysaccharides (dextran), polyethylene glycol, cyclodextrins, chitins, and chitosan, all of which are classified as biopolymers in the present application. The first and second complexing agents are described in columns 5, and 18-19. Preferred embodiments of the first complexing agent include chondroitin sulfates, chitin, chitosan, and various polysaccharides. Column 19, lines 21-24. These overlap with the list of water-soluble polymers, and are also biopolymers according to the present invention. Column 19 of the patent also lists several preferred embodiments of the second complexing agent, defined in the reference as divalent metal cations. Id. Such cationic metals include calcium, magnesium,

and zinc. The reference therefore teaches a microsphere useful for the delivery of therapeutic agents by oral administration comprising a biopolymer and a metal cation.

The reference also specifies some of the therapeutics that may be incorporated as the active agent of the microsphere. These generally include antibiotics, with cephalosporins identified as an example of such an agent. Table 4, column 20; and column 22, lines 1-8. Thus, the reference teaches that cephalosporins may be administered orally in the described microspheres containing a biopolymer and a metal cation. As the reference teaches that the two complexing agents are oppositely charged (column 6, lines 2-5), and that the agents are combined prior to the making of the microsphere (column 5, lines 49-53), it would appear that the agents form ionically bound complexes of the two (thereby meeting the limitations of claim 17).

Further, the cationic metal (the second complexing agent) is described in the patent as "capable of an ionic interaction with a therapeutic agent." Column 5, lines 54-56. As the reference also teaches that the active agent is "loaded into a microsphere" (col. 6, lines 45-48), the reference renders claim 18 obvious. The reference states that the active agent (e.g. cephalosporin) may be loaded into microspheres containing the complexing agents. Thus, the patent teaches that the cephalosporin may be contained by the biopolymer-metal cation complex (the microsphere). Since the metal cation is apparently able to associate both with the active agent and a polymer (the first complexing agent), claim 19 is likewise obvious.

Scott therefore teaches a complex containing a biopolymer and a metal cation that contains a therapeutic, which may be a cephalosporin, that may be used for the oral

administration of the therapeutic. The reference does not however teach the inclusion of an adsorption enhancer in the microsphere.

Watts also teaches a biopolymer composition with a therapeutic agent. Column 3, lines 6-10. Such compositions include microparticles (which includes microspheres). Column 3, lines 61-67. The Watts reference teaches that '[i]t is well known in the literature that the adsorption of polar molecules across mucosal membranes may be greatly improved in they are administered in combination with so-called "absorption enhancers."' It would therefore have been obvious to one of ordinary skill in the art to include an adsorption enhancer in the microsphere of Scott, where such a therapeutic agent, including cephalosporin, was included in the particle. Further, Watts also teaches that among non-ionic surfactants are among the compounds that may be used as absorption enhancers. The motivation to use the absorption enhancer in the microparticle would have been for the same reason that the compounds are known to be useful- they improve the absorption of the therapeutic.

Thus, these two references render the pharmaceutical compositions of the rejected claims obvious. As each of these references have general applicability to cephalosporins (and to other antibiotics), one of ordinary skill in the art would reasonable expect the described compositions to be equally usable with any known cephalosporin. Because the applicant has not indicated any particular reason to choose ceftriaxone, or any of the other identified cephalosporins, and as one of ordinary skill in the art would have had a reasonable expectation of success with any of these compounds, claims 5 and 12 are also obvious.

Neither of these references specifically identifies either pectin or carrageenan as the polymers used in the microparticles. However, both of them are known in the art as useful

polysaccharides for the use in microspheres. See e.g., U.S. Patent 6,315,981, issued to Ungar (column 16, lines 35-41). Further, the Scott reference teaches that polysaccharides may be used in the microsphere described therein. Thus, it would have been obvious to one of ordinary skill in the art to use either of these polysaccharides in the described microspheres.

The limitation of claim 21 is likewise not taught in the disclosed references. However, this is not deemed important as the selection of a particular biopolymer would have been obvious as the selection of the optimal biopolymer. Also, in the specification of the present application, the carrageenan disclosed as meeting the claimed limitation is a known and commercially available carrageenan. Page 24, lines 19-20. It would have been obvious to one of ordinary skill in the art to use a commercially available carrageenan in the composition claimed by the patent.

13. Claims 2, 3, 14, 15, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirai et al., U.S. Patent 4,616,008, in view of Platé et al, U.S. Patent 6,004,583 (of record in the IDS filed on March 25, 2002), and further in view of Watts. The claims, and the teachings of Watts regarding absorption enhancers, are described above.

The Hirai reference teaches a composition comprising cyclodextrin and a lipid soluble cephalosporin intended for oral administration. Abstract. The reference teaches that certain of these cephalosporins may be used as a pharmaceutically acceptable salt formed by an interaction between the cephalosporin and a cationic metal, such as magnesium or calcium. Col. 16, lines 54-62. Thus, the reference teaches a pharmaceutical composition comprising a biopolymer (cyclodextrin), a cephalosporin, and a metal cation. The reference further teaches that the inclusion of the cyclodextrin leads to an increase in the in vivo absorbability of the

cephalosporin. The reference also teaches that other organic acids may be included in the composition to increase the absorption of the cephalosporin. However, the reference does not teach that the cephalosporin is bound to or entrained by the cyclodextrin, or the use of a non-ionic surfactant as an absorption enhancer.

The Platé reference teaches the entrapping of proteins and other 'hard to deliver therapeutics" in a modified hydrogel (comprising polymers including dextrins, col. 18, lines 59-65) such that they may be administered orally. Abstract. The hydrogel of the composition protects the therapeutic from degradation prior to making it available to absorption through the intestinal walls. Cols 6-7. As the reference teaches that the methods taught by this reference may be used with therapeutics other than proteins, it would have been obvious to one of ordinary skill in the art to apply these methods to the administration of cephalosporins when read in combination with Hirai.

Each of the Hirai and the Platé references are concerned with making a therapeutic that is not normally deliverable in an oral composition available for such delivery. Further, each of the references teaches either that a cephalosporin may be included in the respective composition, or that non-peptide therapeutics may be included. Further, each of the references teaches the use of a dextrin polymer to complex with, or entrain the therapeutic. As Hirai does not specify the association between the polymer and the therapeutic, one of ordinary skill in the art would have had a reasonable expectation that combining the compounds of Hirai into the structure taught by Platé would result in an operative composition. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings of Platé with the teachings of the Hirai reference to create a biopolymer/ metal cation/ cephalosporin composition wherein the

cephalosporin was entrapped (entrained) within a biopolymer hydrogel comprising a dextrin. Further, Hirai also teaches the inclusion of an absorption enhancer in the composition, and Watts suggests the use of a non-ionic sulfate as the enhancer. Thus, these references meet all the elements of the claims.

A person reading these references would have been motivated to combine the references to make a composition that would be effective in the oral delivery of cephalosporin to a patient. Oral delivery is known to be preferable in situations where a therapeutic needs to be administered for extended time periods. See e.g., Platé, col. 1, lines 50-55. Thus, the claims identified above are rejected as obvious over Hirai, in view of Platé, and further in view of Watts.

Conclusion

14. The following prior art reference is of record, and is considered pertinent to applicant's disclosure. However, while relevant it is not used as a basis for rejection for the stated reasons.

> Bailey et al., U.S. Patent 6,008,228 (of record in the IDS filed on March 25, 2002). This reference teaches the making of a composition for the oral delivery of a proteinase inhibitor by combining them with an absorption enhancer (capmul) and a biopolymer (fatty acids and PEG). It is relevant in that the combination is made to overcome the same problems of oral delivery with respect to the proteinase inhibitors that are encountered with cephalosporins. Cf., Bailey, cols. 1-2; with Hirai, *supra*, column 1. However, the reference neither indicates that the combination may be used with other compounds, or indicates any binding between the biopolymer and the therapeutic agent, or entrainment of the agent within the biopolymer.

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
March 5, 2003

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